Atrial fibrillation: diagnosis and management—summary of NICE guidance

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[1] National Guideline Centre, Royal College of Physicians, London NW1 4LE, UK

[2] Portsmouth Hospitals University NHS Trust, Portsmouth, UK

[3] NHS England and NHS Improvement, UK

Correspondence to: M Perry
mark.perry@rcp.ac.uk

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GUIDELINES

Atrial fibrillation: diagnosis and management—summary of NICE guidance

Mark Perry, [1] Sophia Kemmis Betty, [1] Nicole Downes, [1] Neil Andrews, [2] Simon Mackenzie[3], on behalf of the Guideline Committee

What you need to know

- Bleeding risk assessment should be used to derive accurate absolute risk scores that can support discussion between clinician and patient about risk modification and appropriate vigilance during anticoagulation. It should not be used to set a threshold for who should be offered anticoagulation
- The ORBIT bleeding prediction tool currently provides the most accurate level of absolute bleeding risk
- Direct-acting oral anticoagulants (DOACs) should be used in preference to warfarin for most patients; the choice of DOAC depends on patient choice and clinical indication
- Radiofrequency point-by-point ablation is the most cost effective treatment for people who have not responded to antiarrhythmic drugs, although laser and cryoballoon ablation may be appropriate in some patients
- Continue anticoagulation after ablation according to risk tools

This article summarises the updated National Institute for Health and Care Excellence (NICE) guideline, *Atrial fibrillation: diagnosis and management*,[1] focusing on three areas where new evidence has led to a change in recommendations: bleeding risk prediction, anticoagulation, and ablation. We explain the Guideline Committee's rationale for these recommendations and highlight challenges to implementation.

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations reproduced here are given in italics in square brackets.

Assessment of bleeding risks

For predicting the need for anticoagulation in people diagnosed with atrial fibrillation, the CHA2DS2-VASc score was retained as the recommended stroke risk tool (fig 1) because it was the most accurate tool for discriminating between those at risk of stroke and those not at risk. In contrast, the choice of tool to assess bleeding risk was less based on discrimination ability and more on the ability to provide an accurate assessment of the absolute risk of bleeding for an individual (box 1), and the Guideline Committee recommends ORBIT for this purpose (box 2).

Box 1: Discrimination and calibration of prediction tools

Discrimination and calibration are both important features in assessing prediction tool performance.

Discrimination

The "discrimination" ability of a prediction tool describes how accurately the tool can categorise people into those at higher and lower risk of an outcome (such as stroke)

- Accuracy of discrimination is measured by observing
  - How many who later get the outcome were correctly designated as higher risk, *and*
  - How many who do not subsequently get the outcome were correctly designated as lower risk.
- Discrimination alone is inadequate to assess a tool's overall predictive ability.

Calibration

The "calibration" ability of a tool describes the agreement between predicted absolute risk and the true (observed) risk in people discriminated into different risk groups. Calibration therefore measures the accuracy of the absolute risk estimates.

- High calibration indicates that the tool's predicted absolute risk is accurate, and is important when an accurate absolute measure of risk is needed. For example, high calibration is relevant when tools are being used to facilitate discussion with the patient about the need for risk modification and vigilance.

The committee agreed that, even if bleeding risk is high, anticoagulation should still be considered for people at risk of stroke. Therefore, a bleeding risk tool should not normally be used to make decisions about who should be anticoagulated. Instead, the tool should be used to provide an accurate assessment of absolute bleeding risk, which can support discussion between patient and clinician, facilitating optimal approaches to anticoagulation. For example, accurate knowledge of bleeding risk may increase compliance with anticoagulation when bleeding risks are low but promote appropriate attention to risk modification during anticoagulation when risk is high. Consequently, a bleeding risk tool's ability to accurately estimate absolute risk—its level of calibration—is more useful than its discriminative capacity.

The committee therefore focused on calibration data for the tools with the most evidence: HAS-BLED, ATRIA, and ORBIT. The calibration evidence clearly suggested that ORBIT was more accurate than HAS-BLED and ATRIA at predicting absolute risk of major bleeding, both for people using vitamin K antagonists and those using direct-acting oral

anticoagulants. Importantly, ORBIT was better calibrated at all, including higher, levels of major bleeding risk. ORBIT was also better at predicting absolute risk of intracranial haemorrhage. All three tools had similar discriminative ability, but ORBIT had a slighter lower sensitivity for major bleeding than the others, and better specificity. The committee concluded that the slight reduction in ORBIT's sensitivity would not be a particular drawback given that ORBIT should not be used to define a binary decision threshold.

Box 2: ORBIT bleeding prediction tool

The ORBIT bleeding prediction tool provides an absolute risk of bleeding, which has been shown to calibrate well with observed incidence of bleeding. An online version can be found at https://www.mdcalc.com/orbit-bleeding-risk-score-atrial-fibrillation.

ORBIT provides an absolute risk quantified by the number of bleeds per 100 patient years. This is based on each patient's sex, haemoglobin (or haematocrit) levels, age, bleeding history, glomerular filtration rate (GFR), and treatment with antiplatelet agents (see table). The absolute risk is calculated from the total score from the points allocated to each binary response.

Characteristic	Possible responses (points allocated)	
Sex	Male	Female
Low haemoglobin or haematocrit*	No (0)	Yes (2)
Age >74 years	No (0)	Yes (1)
Bleeding history†	No (0)	Yes (2)
GFR <60 mL/min/1.73 m2	No (0)	Yes (1)
Treatment with antiplatelet agents	No (0)	Yes (1)

* For males, haemoglobin <13 mg/dL, haematocrit <40%. For females, haemoglobin <12 mg/dL haematocrit <36%.

† Any history of gastrointestinal bleeding, intracranial bleeding, or haemorrhagic stroke.

Each ORBIT score is associated with a discrete absolute risk as shown in the table below:

ORBIT score	Absolute risk (No of bleeds/ 100 patient years (95% CI))
0	1.7 (1.2 to 2.4)
1	2.3 (1.9 to 2.9)
2	2.9 (2.3 to 3.5)
3	4.7 (4.0 to 5.6)
4	6.8 (5.8 to 8.1)
5	9.0 (7.2 to 11.2)
6	12.3 (9.0 to 16.7)
7	14.9 (8.9 to 25.3)

- Assess the risk of bleeding when:
  - Considering starting anticoagulation in people with atrial fibrillation *and*
  - Reviewing people already taking anticoagulation.

  Use the ORBIT bleeding risk score because evidence shows that it has a higher accuracy in predicting absolute bleeding risk than other bleeding risk tools. Accurate knowledge of bleeding risk supports shared decision making and has practical benefits; for example, increasing patient confidence and willingness to accept treatment when risk is low and prompting discussion of risk reduction when risk is high. Although ORBIT is the best tool for this purpose, other bleeding risk tools may need to be used until it is embedded in clinical pathways and electronic systems. [*New guidance.Based on very low to low quality data*]
- Offer monitoring and support to modify risk factors for bleeding, including:
  - Uncontrolled hypertension (see NICE guideline *Hypertension in adults*[2])
  - Poor control of international normalised ratio (INR) in patients taking vitamin K antagonists
  - Concurrent medication, including antiplatelets, selective serotonin reuptake inhibitors (SSRIs), and non-steroidal anti-inflammatory drugs (NSAIDs)
  - Harmful alcohol consumption (see NICE guideline *Alcohol-use disorders*[3])
  - Reversible causes of anaemia.

  [*New guidance. Based on very low to low quality data*]

Anticoagulation to prevent stroke

The committee recommends direct-acting oral anticoagulants (DOACs) because evidence showed that they are more effective than warfarin in preventing harm in people at risk of stroke. There were no studies directly comparing the different DOACs, but indirect comparisons showed that different DOACs offer different benefits depending on the outcome considered. When all these outcomes were combined in the cost effectiveness analysis, apixaban was the most clinically effective and cost effective anticoagulant, based on UK drug tariff prices at the time. However, the Guideline Committee had concerns over the lack of head-to-head comparisons, differences in the study populations, and uncertainties in the economic model, and decided not to recommend one DOAC over the others. Instead they emphasised that DOAC treatment should be tailored to the person's clinical needs and preferences, considering the different risks and benefits of each. The committee agreed that, in the rare circumstances that anticoagulation is not given to people at risk of stroke because of very high bleeding risk, people should have regular review and reconsideration for treatment.

- When deciding between anticoagulation treatment options:
  - Discuss the risks and benefits of different drugs with the person and follow the recommendations on shared decision making in the NICE guideline *Patient experience in adult NHS services*.[4]
  - Follow the recommendations on patient involvement in decisions about medicines in NICE guideline *Medicines adherence*[5] and patient decision aids in *Medicines optimisation*.[6]
  - Take into account any contraindications for each drug and follow the guidance in the *British National Formulary* and the Medicines and Healthcare products Regulatory Agency (MHRA) advice *Direct-acting oral anticoagulants (DOACS)*,[7] in particular for advice on dosages in people with renal impairment, reversal agents, and monitoring.

  [*New guidance.Based on the experience and opinion of the Guideline Committee (GC)*]

- Offer anticoagulation with a direct-acting oral anticoagulant to people with atrial fibrillation and a CHA2DS2-VASc score of 2 or above, taking into account the risk of bleeding. Apixaban, dabigatran, edoxaban, and rivaroxaban are all recommended as options, when used in line with the criteria specified in the relevant NICE technology appraisal guidance (see anticoagulation treatment in the NICE Pathway *Atrial fibrillation overview*[8]). [*New guidance. Based on very low to moderate quality data*]
- Consider anticoagulation with a direct-acting oral anticoagulant for men with atrial fibrillation and a CHA2DS2-VASc score of 1, taking into account the risk of bleeding. Apixaban, dabigatran, edoxaban and rivaroxaban are all recommended as options, when used in line with the criteria specified in the relevant NICE technology appraisal guidance (see anticoagulation treatment in the NICE Pathway *Atrial fibrillation overview*[8]). [*New guidance. Based on very low to moderate quality data*]
- If direct-acting oral anticoagulants are contraindicated, not tolerated, or not suitable in people with atrial fibrillation, offer a vitamin K antagonist. See the section on self monitoring and self management of vitamin K antagonists. [*New guidance. Based on the experience and opinion of the GC*]

Left atrial ablation

No major changes were made to non-ablative treatment recommendations, with rate control drugs recommended as the first line approach, followed by antiarrhythmic drug treatment if rate control drugs are unsuccessful. Ablation may be a treatment option if antiarrhythmic drug treatment has not been successful or is not tolerated (fig 2), and new evidence showed that the catheter ablation techniques (radiofrequency point-by-point, radiofrequency multi-electrode, laser, and cryoballoon) are the most clinically effective ablation options. These techniques have similar efficacy to each other, each generating a marked reduction in the rate of atrial fibrillation recurrence compared with medical treatment, while having a rate of serious adverse events similar to medical treatment. Thoracoscopy and the hybrid techniques lead to even lower atrial fibrillation recurrence, but they also lead to more serious adverse effects.

A new economic model developed for the guideline that used the clinical evidence from people with paroxysmal atrial fibrillation showed that radiofrequency point-by-point ablation was more cost effective over a lifetime than antiarrhythmic drug treatment and other ablation strategies in people for whom one or more antiarrhythmic drug had failed.

Cryoballoon, radiofrequency multi-electrode, and laser ablation were the second, third, and fourth most cost effective options respectively. Despite further analysis to account for possible inaccuracies in NHS reference costs, radiofrequency point-by-point ablation remained the most cost effective option, and other catheter ablation techniques are therefore unlikely to provide a cost effective use of NHS resources. Based on the economic model results, the committee agreed that radiofrequency point-by-point ablation should be considered in people with symptomatic paroxysmal atrial fibrillation if drug treatment is unsuccessful, unsuitable, or not tolerated.

Cryoballoon and laser ablation may sometimes be more suitable for some patients because they may be carried out without general anaesthesia, and cryoballoon ablation may be quicker, with same day discharge more likely. There is also a risk of fluid overload from saline irrigated radiofrequency ablation. The committee therefore decided that either cryoballoon or laser ablation could be considered if radiofrequency point-by-point ablation is not suitable. Radiofrequency multi-electrode was not included as an alternative due to its lower efficacy relative to cryoballoon and laser ablation and concerns about a higher risk of stroke.

There was limited direct evidence for ablation in people with persistent atrial fibrillation, but the committee decided that it was sufficient to support radiofrequency point by point ablation (or cryoballoon and laser ablation in the special circumstances outlined above) as an option to be considered for those with persistent symptoms that are unrelieved by antiarrhythmic drugs.

While evidence showed that ablation may reduce symptoms and improve quality of life there was no evidence that it significantly reduces serious clinical events such as stroke, heart failure, or death. Consequently, the decision to stop anticoagulation after ablation should be based on stroke and bleeding risk assessed using CHA2DS2-VASc and ORBIT as for all other patients with AF.

- If drug treatment is unsuccessful, unsuitable, or not tolerated in people with symptomatic paroxysmal or persistent atrial fibrillation:
  - Consider radiofrequency point-by-point ablation *or*
  - If radiofrequency point-by-point ablation is assessed as being unsuitable, consider cryoballoon ablation or laser balloon ablation.

  [*New guidance. Based on very low to low quality data*]
- When considering left atrial ablation, discuss the risks and benefits and take into account the person's preferences. In particular, explain that the procedure is not always effective and that the resolution of symptoms may not be long lasting. [*New guidance. Based on very low to low quality data*]
- Base decisions to stop anticoagulation on a reassessment of stroke and bleeding risk using CHA2DS2-VASc and ORBIT and a discussion of the person's preferences. [*New guidance. Based on very low quality data*]

Implementation

There are three main areas where implementation challenges exist. Firstly, the use of the ORBIT score is a change in practice, which may require some re-education in primary and secondary care, and ORBIT will need to become embedded in GP systems. Secondly, the recommendations on anticoagulation are likely to lead to an increase in use of direct-acting oral anticoagulants (DOACs), as part of an ongoing trend. The unit cost of DOACs is greater than that for warfarin, so there is likely to be a resource impact. Finally, recommendations on ablation are likely to lead to a change in the types of ablation offered, with more people receiving radiofrequency point-by-point ablation and fewer having other catheter ablation techniques.

Future research

During guideline development, evidence relating to new diagnostic methods was not strong enough to permit new recommendations. Alongside the research recommendations made in other areas, the following research recommendations for diagnostic methods were made:

- What is the diagnostic accuracy of key index tests (such as the KardiaMobile heart monitor (AliveCor), MyDiagnostik, Microlife BP monitors, iPhone plethysmography, and pulse palpation) compared with the gold standard of 12-lead electrocardiography in people with risk factors for or symptoms of atrial fibrillation?

- What is the diagnostic accuracy of key index tests compared with the gold standard of prolonged ambulatory monitoring in people suspected of having paroxysmal atrial fibrillation?

Guidelines into practice

- How can an accurate knowledge of a patient's absolute risk of bleeding be used to facilitate discussion about risk factor modification with a patient who needs anticoagulation?
- How would you explain the potential benefits and harms of radiofrequency ablation to a symptomatic patient who has not responded to anti-arrhythmic drugs?

How patients were involved in the creation of this article

Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here.

Further information on the guidance

This guidance was developed by the National Guideline Centre in accordance with NICE guideline methodology (www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf). A guideline committee (GC) was established by the National Guideline Centre, which incorporated healthcare and allied healthcare professionals (one medical director for system improvement and professional standards, two consultant cardiologists and electrophysiologists, one cardiovascular research pharmacist and principal pharmacist, one strategic lead for MSc Advanced Practice, one GP principal, one chair of geriatrics and stroke medicine and consultant in stroke medicine, one acute medicine, diabetes and clinical pharmacology consultant, one clinical associate professor in primary care and head of undergraduate primary care education, one arrythmia nurse specialist, one chair in cardiovascular medicine and cardiology consultant) and two lay members.

The GC identified relevant review questions and collected and appraised clinical and cost effectiveness evidence. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes or themes rather than the quality of the study. The GC agreed recommendations for clinical practice based on the available evidence or, when evidence was not found or evidence was conflicting, based on their experience and opinion using informal consensus methods.

The scope and the draft of the guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the GC took comments into consideration when producing the final version of the guideline.

The short version of the guideline, which includes the full list of recommendations and their rationales and impacts, is available on the NICE website in the Guidance section (https://www.nice.org.uk/guidance/ng196). The evidence reviews, which provide the evidence underpinning the recommendations and the GC discussion of the evidence, are available in the Evidence section (https://www.nice.org.uk/guidance/ng196/evidence).

NICE will conduct regular reviews after publication of the guidance to determine whether the evidence base has progressed significantly enough to alter the current guideline recommendations and require an update.

Contributors: All authors made substantial contributions to the conception or design of the work, as well as the interpretation of data for the work. They all revised the work critically for important intellectual content, approved the final version for publication, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are investigated and resolved. MP wrote the first draft, and MP, SKB, and ND made substantial contributions to the acquisition and interpretation of data for the work. MP is responsible for the overall content as guarantor.

Essential contributors included the NICE Guidelines Technical Support Unit (Department of Population Health Sciences, Bristol Medical School), which helped produce the anticoagulation model; Dr Sharon Swain, who directed the guideline; Dr Giulia Zuodar who managed the guideline; and Mrs Elizabeth Pearton who carried out the literature searches. The guideline members contributed significantly to the intellectual content of this guideline.

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The members of the Guideline Committee were (shown alphabetically): Neil Andrews, Matthew Bates, Antony Chuter, Nazish Khan, Paulus Kirchhof, Geraldine Lee, Simon Mackenzie, Thomas McAnea, Irene McGill, Chakravarthi Rajkumar, Yohan Samarasinghe, Jaspal Taggar, Keith Tyndall.

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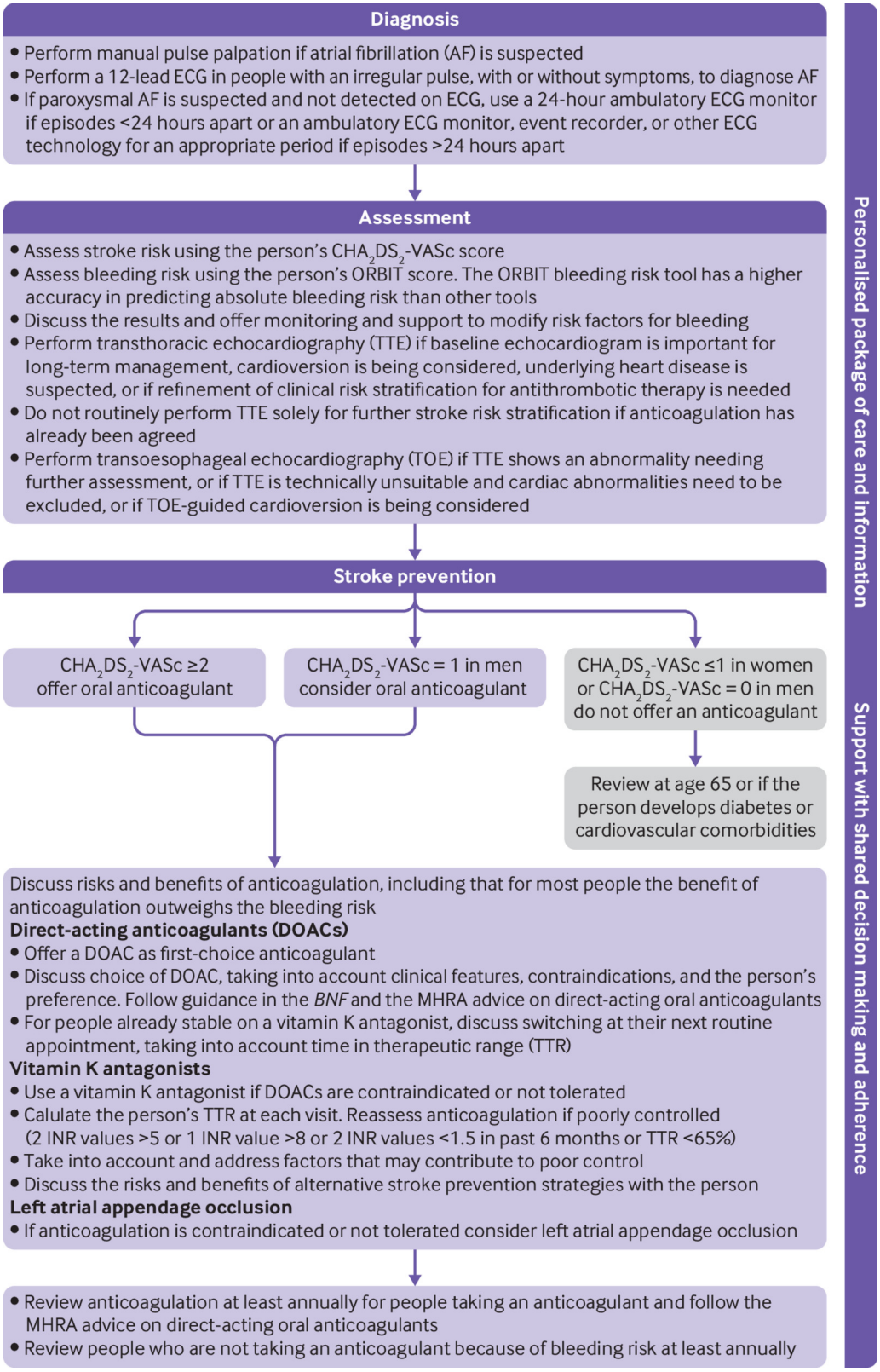

Fig 1 | Algorithm for diagnosis and assessment of atrial fibrillation and prevention of stroke (excerpt from NICE guideline *Atrial fibrillation: diagnosis and management*[1])

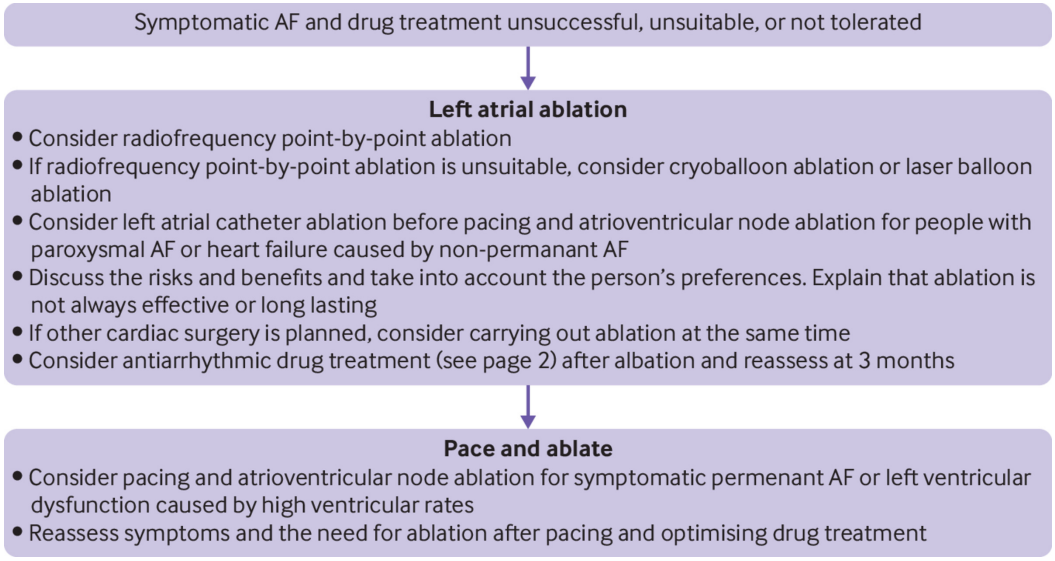

Fig 2 | Algorithm for left atrial ablation strategies (excerpt from NICE guideline *Atrial fibrillation: diagnosis and management*[1])